

### **REMARKS**

Applicant respectfully requests reconsideration. Claims 1, 3, 4, 6, 7, 9-16 and 20-55 were previously pending in this application. By this amendment, Applicant is cancelling claims 38-54 without prejudice or disclaimer. No claims have been amended, and no new claims have been added. As a result, claims 1, 3, 4, 6, 7, 9-16 and 20-37 are pending for examination with claims 1, 4 and 7 being independent claims. No new matter has been added.

#### **Rejections Under 35 U.S.C. §102**

Claims 44-46, 48-50, and 52-54 are rejected under 35 U.S.C. § 102(b) as being anticipated by WO 01/66557 (published 13 September 2001/IDS reference number 3 submitted May 25, 2010).

Without conceding the correctness of the rejection, and solely to expedite prosecution, Applicant has cancelled claims 44-46, 48-50, and 52-54 rendering the rejection moot.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 38-43, 44-49, 51-53, and 55 are rejected under 35 U.S.C. § 102(e) as being anticipated by Berger et al. (US Patent Application Publication No. 2003/0148410 A1).

Without conceding the correctness of the rejection, and solely to expedite prosecution, Applicant has cancelled claims 38-43, 44-49, 51-53, and 55 rendering the rejection moot.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

#### **Rejections Under 35 U.S.C. §103**

Claims 1, 3, 4, 6, 7, 9-16, 20-49, 51-53, and 55 are rejected under 35 U.S.C. §103(a) as being unpatentable over Iba et al. (Am J. Pathol. 154(5): 1489-501, May 1999), and further in view of Berger et al. (U.S. Patent Application Publication No. 2003/0148410 A1).

According to the Office Action, “[a]pplicants have not presented any scientific evidence that teaches away from one of ordinary skill in the art implementing tissue samples to assess ADAM12 expression and diagnosing epithelial cancers.” (page 5 of the Office Action).

Applicant respectfully disagrees and requests reconsideration of this rejection. “The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the

claimed invention would have been obvious.” (see MPEP § 2142). MPEP § 2143.02 and established case law states that “[t]he prior art can be modified or combined to reject claims as prima facie obvious as long as there is a reasonable expectation of success. In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986)” (emphasis added).

Iba et al. dissuades one of ordinary skill in the art from detecting the presence of ADAM 12 using the instantly claimed biological fluids obtained from a cancer patient. Iba et al. measured the distribution of ADAM 12 in a series of 37 tissue specimens from histologically confirmed cases of human carcinomas. According to Iba et al. the membrane-anchored form of ADAM 12 (ADAM 12-L) is up-regulated in breast carcinoma tissues while, the secreted form (ADAM 12-S) is present in both normal and tumor tissue. Because the secreted form of ADAM 12 does not differentiate between cancer and normal tissues, while the membrane-bound form of ADAM 12 is not expected to be present in biological fluids, one of ordinary skill in the art would not have any expectation of success in diagnosing cancers of epithelial origin by detecting ADAM 12 in biological fluids. In light of these teachings, a skilled artisan would conclude that neither form of ADAM 12 can be used in a method for detecting and characterizing cancers of epithelial origin using the biological fluids recited in the instant claims.

The substitution of various tumor tissue samples taught by Iba et al. with the colon-associated fluids of Berger et al. would not have yielded a predictable result. Based on the teachings of the cited prior art, a skilled artisan would conclude that ADAM 12 cannot be used in a method directed to the detection and/or characterization of cancer using body fluids because the secreted form of ADAM 12 cannot differentiate between normal and tumor tissue.

The Office Action states that “Berger teaches assaying samples in general for the diagnosis of not only colon cancer, but ovarian, lung, cervical, breast and prostate cancer as well” (page 6 of the Office Action).

“[A] patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art”. KSR Int’l v. Teleflex Inc., 82 USPQ2d 1385, 1396 (2007). “The fact that a claimed product is within the broad field of the prior art and one might arrive at it by selecting specific items and conditions does not render the product

obvious in the absence of some directions or reasons for making such selection.” Ex parte Kuhn, 132 USPQ2d 1958 (Bd App 1961).

Berger et al. is focused on the use of colon cells and colon-associated fluids for detecting colon cancer. The instant claims exclude detection of colon cancers. Berger et al. has not provided any reason for detecting cancers of epithelial origin, other than colon cancer, using the biological samples recited in the instant claims. As explained above, in light of the teachings of Iba et al., a skilled artisan would conclude that ADAM 12 cannot be used in a method directed to the detection and/or characterization of cancer using body fluids since the secreted form of ADAM 12 cannot differentiate between normal and tumor tissue. MPEP §2141.02(VI) clearly sets forth that “a prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention (emphasis original). By ignoring the converse teaching of Iba et al., the Office is selectively focusing on certain teachings of the prior art and ignoring others.

The Office Action asserts that “Applicants’ claims do not include an antibody that differentiates between the two forms of ADAM 12. For these reasons and the reasons of record the rejection is made and maintained.” (page 6 of the Office Action).

Applicant respectfully reiterates that, based on the teachings of the cited art, a skilled artisan would conclude that neither form of ADAM 12 can be used in a method directed to the detection and characterization of cancer using the instantly claimed biological samples. Accordingly, Applicant should not be required to limit the claims to any particular species of ADAM 12.

In conclusion, because the prior art combination would not have yielded predictable results to one of ordinary skill in the art, the cited references do not render the instant claims obvious.

Accordingly, withdrawal of this rejection is respectfully requested.

Claims 1, 3, 4, 6, 7, 9-16, 20-49, 51-53, and 55 are rejected under 35 U.S.C. §103(a) as being unpatentable over Iba et al. (Am J. Pathol. 154(5): 1489-501, May 1999), and further in view of WO 01/66557 (published 13 September 2001/IDS reference number 3 submitted May 25, 2010) and Berger et al. (U.S. Patent Application Publication No. 2003/0148410 A1).

The Office Action contends that “[i]t would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine all the teachings of

all the documents to assay a plethora of biological samples for ADAM 12 particularly a urine, blood or serum”, and that “[o]ne of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Berger” (page 8 of the Office Action).

Applicant respectfully disagrees and requests reconsideration of this rejection. As discussed in response to the previous obviousness rejection, in light of the teachings of Iba et al., a skilled artisan would conclude that ADAM 12 cannot be used in a method directed to the detection and/or characterization of cancer using body fluids since the secreted form of ADAM 12 cannot differentiate between normal and tumor tissue. These deficiencies are not addressed by Berger et al. (discussed above) and /or WO 01/66557.

WO 01/66557 relates to ADAM polypeptides, isolated nucleic acids and antibodies. According to the Office Action, the WO document teaches that antibodies directed to the ADAM 12 protein are used for the diagnosis of cancers, such as gastric, ovarian, lung, liver, breast and bladder, in a biological sample, which includes body fluids and tissue biopsies (page 7 of the Office Action).

Applicant respectfully disagrees. As discussed above, established case law states that “[t]he fact that a claimed product is within the broad field of the prior art and one might arrive at it by selecting specific items and conditions does not render the product obvious in the absence of some directions or reasons for making such selection.” Ex parte Kuhn, 132 USPQ2d 1958 (Bd App 1961). Furthermore, the Office is not entitled to use the claim as a “frame” and to employ “individual, naked parts of separate prior art references...as a mosaic to recreate a facsimile of the claimed invention.” W. L. Gore & Assoc., Inc. v. Garlock, Inc., 721 F.2d 1540, 1552 (Fed. Cir., 1984). WO 01/66557 does not teach a method for detecting cancers of epithelial origin using the instantly claimed biological samples.

In conclusion, because the prior art combination would not have yielded predictable results to one of ordinary skill in the art, the cited references do not render the instant claims obvious.

Accordingly, withdrawal of this rejection is respectfully requested.

#### Double Patenting Rejection

Claims 1, 3, 4, 6, 7, 9-16, 20-43, 44, 45, 48, 49, 52 and 53 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21, 23

and 42 of copending Application No. 12/085,134 (US Patent Application Publication No. 2009/0215102).

The rejection is a provisional one since claims 21, 23 and 42 of copending Application No. 12/085,134 have not been found allowable. Applicant respectfully requests that this rejection be held in abeyance until an indication of allowable subject matter is received.

**CONCLUSION**

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. C1285.70006US01.

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Respectfully submitted,

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